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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,156	FEDER ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) *33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-32 and 34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *21-32 and 34-40* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and Claims:

The Information Disclosure Statement, filed 1/16/03, has been entered into the record. Applicant's election of Invention I in Paper No. 7 (1/16/03) is acknowledged. Claims 1-20 have been cancelled. Claims 21-40 have been added and read on the elected Invention.

It should be noted that claims will be examined insofar as they read on the elected Invention and Species. Claim 33 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected Invention, there being no allowable generic or linking claim. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Furthermore, cancellation of the non-elected Species in Claims 1-20 and addition of Claims that read only on SEQ ID NO: 23, is taken as an election of Species without traverse based on an incomplete response (see the Office Action of 12/20/02).

Claims 21-32 and 34-40 are under examination in the instant Application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

Sequence Rules

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules is

not accompanied by the required reference to the relevant sequence identifier (i.e., SEQ ID NO:). This happens in Figures 1, 2, 6 and 7, for example.

URL's

The disclosure is objected to because it contains browser-executable code. This occurs, for example, on p. 244, line 12. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only (e.g., "The Genewise/Wise2 Package"). See MPEP § 608.01 (p).

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of 35 U.S.C. 101:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 21-32 and 34-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well-established utility. Novel biological molecules lack established utility and must undergo extensive experimentation.

The claims are directed to a nucleotide encoding a potassium channel subunit and nucleotides having at least 60% sequence homology to SEQ ID NO: 23. Further, the claims recite an expression vector comprising the nucleic acid molecule (SEQ ID NO:23) that produces a potassium channel subunit as well as methods of recombinantly producing the channel. However, very little information is known about the channel except the sequence data, and no function has been attributed to it. The instant specification suggests similarities to potassium ion channels. However, the specification does not disclose the function of the ion-channel-like polypeptide in the context of the cell or organism. The applicant does not disclose any modulatory function, nor any diseases or conditions associated with altered levels or forms of the ion-channel-like polypeptide or its putative ligands. Significant further experimentation would be required of the skilled artisan to identify *any* function associated with the ion-channel-like polypeptide or the polynucleotide encoding it.

No well-established utility exists for newly isolated, complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed polynucleotide(s) or for the polypeptide encoded by the polynucleotide of SEQ ID NO: 23.

1) To produce molecules useful for the treatment of potassium ion-channel polypeptide deficiency.
2) For the production of antibodies.
3) To produce a variant nucleotide and polypeptide.
4) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide.

5) In tissue typing.

Each of these shall be addressed in turn:

1) *To produce molecules useful for the treatment of potassium ion-channel polypeptide deficiency.* This asserted utility is credible and specific, however, it is not substantial. The specification does not disclose any conditions wherein there is a deficiency of the claimed polynucleotides or polypeptides. Significant further experimentation would be required of the skilled artisan to identify individuals who would benefit from such a compound, and then to determine a best course of treatment. There is no disclosure, for example, of dosages, how to assay for improvement or intolerable levels of side effects, etc. Since this asserted utility is not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) *For the production of antibodies.* This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, both the polypeptide and its antibodies have no patentable utility.

3) *To produce a variant nucleotide and polypeptide.* This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Further, the specification discloses nothing specific or substantial for the variant nucleotide and polypeptide that is produced by this method. Since this asserted utility is also not present

in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide. This asserted utility is credible and specific. However, it is not substantial. The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure for example, of how to assay for ligand binding and possible transduction mechanisms. It is not known the class of drugs to use or what measurements to perform. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not substantial.

5) *In tissue typing.* This asserted utility is credible but not substantial or specific. Such assays can be performed with any polypeptide encoded by a polynucleotide; thus the asserted utility is not specific. Furthermore, the specification discloses a wide range of tissues that express the polypeptide of SEQ ID NO: 24. Applicants have demonstrated that the polypeptide of SEQ ID NO: 4 in the instant application is expressed in various tissues, including the testis, liver, small intestine, spinal cord, breast, etc. Applicant implies that this expression supports a useful function of the polynucleotide encoding SEQ ID NO: 24. However, patentable utility of tissue typing for the polynucleotide encoding the claimed polypeptide is not substantial because one skilled in the art would not readily use the nucleotide sequences for tissue-typing in a real world sense as the protein is not specific to one tissue and is not associated with any disease or disorder. This asserted utility is also not specific because numerous unrelated nucleotide

sequences would also show a similar tissue typing pattern. In addition, evidence of mere expression in a tissue is not tantamount to a showing of a role for the polynucleotide of the present invention. It is not clear if expression of the polynucleotide of the present Invention is correlated with a specific change in physiology, for example, or with a disease state. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Claims 21-32 and 34-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 21-32 and 34-40 are directed to an isolated nucleic acid molecule (SEQ ID NO: 23) that encodes a potassium channel subunit polypeptide. Further, the claims recite an expression vector comprising the nucleic acid molecule that produces the ion-channel-like polypeptide, a recombinant host cell, hybridizing polynucleotides, and a process of producing a recombinant host cell and polypeptide.

The specification teaches the polynucleotide encoding the ion-channel-like polypeptide. However, the specification does not teach functional or structural characteristics of the claimed polynucleotide or ion-channel-like polypeptide recited in the claims.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al.

(2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Furthermore, the specification asserts that the claimed polynucleotide encodes an ion channel protein based on homology to known ion channels. This assertion cannot be accepted as credible in the absence of supporting evidence of specific function, because the art shows that structurally similar ion channels are unpredictably functionally dissimilar. For example, relevant literature reports that potassium channels constitute the most diverse class of ion channels with respect to kinetic properties, regulation, pharmacology, and structure (pg. 1329; Lehmann-Horn et al. Physiol Rev 79 (4): 1317-1372).

Additionally, over 50 distinct channels have been identified in humans in both excitable and non-excitable cell types. The channels are involved in the control of a variety of cellular functions, including neuronal firing, cellular proliferation, and neurotransmitter and hormone secretion.

Although ion channel family members share several common structural features, relevant art (pg 1329-1330; Lehmann-Horn et al. Physiol Rev 79(4): 1317-1372, 1999) shows that members of a class do not always share a specific and substantial functional attribute or utility, despite having structural features in common. Therefore, membership in a class of ion channels may not impart a specific, substantial, and credible utility to a new member, such as the claimed polynucleotide of the instant Application.

Based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotides to make a biologically active ion channel-like polypeptide without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polynucleotides encoding the ion channel-like polypeptide for any purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polynucleotides encoding the ion channel-like polypeptide could be used as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides for any purpose.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polynucleotides encoding the ion channel-like polypeptide and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Furthermore, regarding Claims 37-40, the specification does not enable variants of SEQ ID NO: 23. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims.

The claims are directed to the polynucleotide and variants of SEQ ID NO: 23. Claims 37-40 read on nucleotides that are at least 60% identical to SEQ ID NO: 23. The scope of the patent protection sought by the Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

The Instant Application does not reasonably provide enablement for various nucleotide forms of SEQ ID NO: 23, wherein the sequence is at least 60% identical to the nucleotide of SEQ ID NO: 23. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in

scope with these claims. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The specification is not enabled for the full scope of Claims 37-40, wherein the nucleotide sequence is 60% identical to SEQ ID NO: 1, with the assurance that enabled polynucleotides can be made without undue experimentation and with the assurance that they would have the desired properties. There are no examples of what specific polynucleotides fall within the range of those that would be 60% identical. Neither is it clear if this percent identity need be over a contiguous region or a specific portion of the protein. Claims 37-40 encompass numerous undefined variants of SEQ ID NO: 23. However, as discussed above, it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10

USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "complimentary", and the claim also recites "antisense" which is the narrower statement of the range/limitation.

Furthermore, Claim 21 is rendered indefinite for reciting the phrase "corresponding to." It is not clear what is meant by this phrase in the context of expression of a protein. It is not known if a "polypeptide *corresponding* to amino acids 146 to 241" is identical to or similar to a specific sequence.

Claim 21 is rendered indefinite because of the phrase "stringent conditions," which is a conditional term. The metes and bounds of the claim cannot be ascertained. This rejection can be overcome by supplying specific conditions supported by the specification, which the Applicants consider "stringent."

Claims 37-40 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 37-40 are directed to an isolated nucleic acid molecule (SEQ ID NO: 23) that encodes a potassium ion channel polypeptide. Further, the claims recite an expression vector comprising the nucleic acid molecule that produces the polypeptide, a recombinant host cell, variants, and heterologous sequences, as well as a process of producing a recombinant host cell and polypeptide.

The specification teaches a polynucleotide (SEQ ID NO: 23). However, the specification does not teach functional or structural characteristics of the claimed polynucleotides. The description of one polynucleotide encoding a potassium channel polypeptide (SEQ ID NO: 23) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid

itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 23 which encodes a full-length polypeptide, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be

reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623. Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

2/10/03

Elizabeth C. Kemmerer

[redacted]